UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/524,454	03/10/2000	Kristian Berg	697.013US1	5804

21186 7590 04/01/2005

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
P.O. BOX 2938
MINNEAPOLIS, MN 55402

EXAMINER	
EWOLDT, GERALD R	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 04/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/524,454	BERG ET AL.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-11,22 and 23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-11 and 22-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment and remarks, filed 12/27/04, are acknowledged. Upon reconsideration, the previous rejection under the first paragraph of 35 U.S.C. § 112 for the introduction of new matter into the claims has been withdrawn.

2. Claims 2-11 and newly added Claims 22 and 23 are pending and being acted being acted upon.

3. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 2-11 and newly added Claims 22 and 23 stand/are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the specification provides insufficient evidence that the claimed method could be used for expressing a molecule on a cell, said method comprising photochemical internalization wherein the molecule is sufficient to generate an immune response, for the reasons of record as set forth in the papers mailed 4/24/01, 6/18/02, 2/10/03, 1/24/03, and 8/23/04.

As set forth previously, the breadth of the claims, in light of the limited disclosure of the specification, would not allow one of skill in the art to practice the invention as broadly claimed without an undue amount of experimentation.

First note that it is clear that the photochemical method (employing certain disclosed agents) of the instant application (and the prior art) can be used to internalize exogenous molecules. The method of the instant claims, however, requires more. The claimed method requires the surface presentation of a sufficient amount of the internalized molecule to generate an immune response. Indeed, Claim 11 actually recites the stimulation of said response.

It is well-known in the immunological arts that only certain antigen presenting cells are capable of presenting antigens and generating an immune response. See, for example, Janeway et al. (1994) wherein it is taught that in addition to antigen presentation, costimulation that can only be provided by B cells, macrophages, or dendritic cells, is required for the generation of an immune response. Accordingly, it appears that the method of Claims 2-5 and 7-11, employing any cell capable of

photochemical internalization, could not be performed without an undue amount of experimentation.

Further regarding the breadth of the claims, the specification discloses only the actual use of $AlPcS_{2a}$ and $TPPS_{2a}$ as photochemical internalization agents. Claims 2-7 and 9-11 comprise either no limitations regarding photochemical internalization agents, or as in the case of Claim 7, are drawn to whole classes of agents including "derivatives thereof". The disclosure of two related species of agents cannot be considered to be reasonably sufficient to enable the method of the instant claims to be performed with any of the essentially unlimited number of disclosed families of chemicals (and derivatives thereof) without an undue amount of experimentation.

Finally, it remains the Examiner's position that the disclosure of the specification does not sufficiently demonstrate the required limitation that the claimed method be capable of inducing sufficient MHC class I presentation of an antigen to generate an immune response. As set forth previously, the specification fails to disclose any actual Class I MHC presentation. Indeed, the only experiment which might demonstrate any sort of surface presentation, Example 3, clearly demonstrates the opposite, the triangles of Figure 4 show a *lack* of antigen on the surface of the cells.

Applicant's arguments, filed 12/27/04 have been fully considered but they are not persuasive. Applicant argues that because the Examiner has stipulated that the method of Example 2 is enabled, the method of the instant claims is enabled. Applicant further argues that the specification enables a variety of cell types that can generate an immune response. Applicant states "Applicants contemplate as antigen-presenting any cell capable of expressing or presenting on its surface a molecule that is administered or transported into its cytosol".

In regards to Example 2, the methods of the example are not the methods of the instant claims, nor are they representative of the scope of the methods of the instant claims. In the example, a single cell type is loaded with a particular antigen; said loaded cell is then used in a CTL ^{51}Cr release assay. The CTLs employed in a ^{51}Cr assay are primed/activated CTLs and are not representative of the generation or stimulation of an immune response, i.e., the method of the instant claims. See, for example, Janeway et al. (1994) wherein one of the fundamental rules of cellular immunology is taught, i.e., that the generation of an immune response from naïve T cells *requires* professional APCs. Clearly then, the ^{51}Cr assay of Example 2 employs primed/activated CTLs and does not comprise the generation or stimulation of an immune response. Note also that the specification discloses that the assay of Example 2 is the assay of Fossum et al. (1995) in which primed CTLs were employed. Accordingly, it remains the Examiner's position that given the breadth of the claimed method, i.e., the employment of *any* cell type in the production of cells capable of generating

an immune response (in defiance of one of the fundamental concepts of cellular immunology), the specification provides insufficient support and is not enabling. Clearly, the method of the instant claims must be considered to be highly unpredictable and requiring of undue experimentation to practice as claimed.

Applicant argues that the specification discloses several different photosensitizers of unrelated classes.

Applicant's statement is true. However, the mere assertion that several unrelated agents function in a method that is highly unpredictable is not in itself enabling. As set forth previously, the specification discloses only the actual use of $AlPcS_{2a}$ and $TPPS_{2a}$, and then only as photochemical internalization agents; the mere fact that these agents can get an antigen into a cell does not reasonably demonstrate that the cell is then capable of generating an immune response.

Applicant argues that Example 3 illustrates the transport of HRP from the cytosol.

It appears to the Examiner that the Example may illustrate transport of HRP *into* the cytosol, but this is not the unpredictable portion of the method of the instant claims.

5. Claim 7 stands rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

There is insufficient written description to show that Applicant was in possession of "a lysomotropic weak base" of "a porphyrin, phthalocyanine, purpurin, chlorin, benzoporphyrin, naphthalocyanine, cationic dye, or tetracycline".

As set forth previously, "the specification fails to disclose any species of the claimed reagents. Further, no definition is provided that would limit "lysomotropic weak bases". Accordingly, one of skill in the art would conclude that the specification fails to disclose a representative number of species to describe the claimed genus.

Applicant's arguments, filed 12/27/04 have been fully considered but they are not persuasive. Applicant argues that

the phrase is well-known in the art and submits several references in support.

Whether or not generic lysomotropic weak bases were well-known in the art is not the issue at hand. The issue is whether or not lysomotropic weak bases of a porphyrin, phthalocyanine, purpurin, chlorin, benzoporphyrin, naphthalocyanine, cationic dye, or tetracycline were well-known in the art. A review of the references fails to show that the lysomotropic weak bases in question were well-known in the art as they are not the subjects of the references.

6. The following are new grounds for rejection,

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-10 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by WO96/07432 (IDS).

WO96/07432 teaches a method of expressing an antigenic molecule on the surface of a viable cancer cell, said method comprising:

contacting said cell *in vitro* with said antigenic molecule (including a vaccine component, a molecule capable of stimulating an immune response, and a peptide, also including an antigen bound to a carrier molecule) and with a photosensitizing agent (a porphyrin, phthalocyanine, purpurin, chlorin, benzoporphyrin, naphthalocyanine, cationic dye, tetracycline, and a lysomotropic weak base thereof, including $TPPS_4$, $TPPS_{2a}$, and $AlPcS_{2a}$, also including a photosensitizing agent bound to a carrier molecule),

wherein said molecule and said agent are each taken up into an intracellular membrane-restricted compartment of said cell; and irradiating said cell with light of a wavelength effective to activate the photosensitizing agent, such that the membrane of said intracellular compartment is disrupted, releasing said molecule into the cytosol of the cell, without killing the cell by irradiation,

wherein, said released antigenic molecule, or a part thereof of sufficient size to generate an immune response, is

subsequently presented on the surface of said cell by a class I MHC molecule (see particularly the claims). Note that reference does not specifically state that the method results in the cell surface expression of the antigen in MHC Class I, however, the reference teaches the same steps as those of the instant claims, thus, said same steps would inherently result in the same outcome, i.e., the claimed method of the expressing an antigenic molecule on the surface of a viable cell.

The reference clearly anticipates the claimed invention.

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

11. **Please Note**: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

3/22/05

G.R. Ewoldt, Ph.D.
Primary Examiner
Technology Center 1600